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FILE 'MEDLINE, EMBASE, SCISEARCH, BIOSIS, USPATFULL' ENTERED AT 12:25:59 ON 09 JUL 2002

L1 18594 S (NO OR (NITRIC OXIDE)) (6P) (PROTOZOA? OR PLASMODIUM OR LEISH
L2 243153 S (NO OR (NITRIC OXIDE)) (P) (BREATH? OR INHAL? OR GASEOUS OR G
L3 363 S L1 (6P) L2
L4 362 S L1 (3P) L2
L5 361 S L1 (P) L2
L6 184 DUP REM L5 (177 DUPLICATES REMOVED)
L7 20795 S (NITRIC OXIDE) (P) (BREATH? OR INHAL? OR GASEOUS OR GAS OR RE
L8 58 S L1 (6P) L7
L9 37 DUP REM L8 (21 DUPLICATES REMOVED)
L10 10281 S (NITRIC OXIDE) (6P) (BREATH? OR INHAL?)
L11 13 S L1 (6P) L10
L12 11 DUP REM L11 (2 DUPLICATES REMOVED)
L13 26 S L1 AND L10
L14 24 DUP REM L13 (2 DUPLICATES REMOVED)
L15 9491 S ((NITROUS OR NITRIC) (A) OXIDE?) (3A) (BREATH? OR INHAL? OR R
L16 7 S L15 (6P) L1
L17 2 DUP REM L16 (5 DUPLICATES REMOVED)
L18 8 S L15 AND L1
L19 3 DUP REM L18 (5 DUPLICATES REMOVED)

ANSWER 18 OF 37 MEDLINE DUPLICATE 3

ACCESSION NUMBER: 2000244894 MEDLINE
DOCUMENT NUMBER: 20244894 PubMed ID: 10784308
TITLE: Experiences with severe P. falciparum malaria in the intensive care unit.
AUTHOR: Losert H; Schmid K; Wilfing A; Winkler S; Staudinger T; Kletzmayr J; Burgmann H
CORPORATE SOURCE: Department of Internal Medicine I, University Hospital of Vienna, Austria.
SOURCE: INTENSIVE CARE MEDICINE, (2000 Feb) 26 (2) 195-201. Journal code: 7704851. ISSN: 0342-4642.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000728
Last Updated on STN: 20000728
Entered Medline: 20000720

AB OBJECTIVE: To review the clinical profiles and therapies instituted for patients with severe malaria admitted to an ICU. DESIGN: Retrospective study. SETTING: Internal ICU of a tertiary care centre. PATIENTS AND PARTICIPANTS: Between January, 1992, and February, 1999, 104 patients with malaria were admitted to the General Hospital of Vienna. Sixty-nine patients suffered from **Plasmodium** falciparum malaria (66%), seven of these were admitted to the ICU. MEASUREMENT AND RESULTS: Seven patients were admitted to the ICU, of whom three died (4% in hospital case-fatality rate). Four patients required mechanical ventilation because of **respiratory** insufficiency and adult **respiratory** distress syndrome (ARDS), of whom three died. Three patients were treated with **inhaled nitric oxide** (**NO**) and kinetic therapy; one patient required extracorporeal veno-venous oxygenation. All patients who died required haemofiltration because of acute renal failure. CONCLUSION: As P. falciparum is a potentially life-threatening disease, reliable criteria for ICU admission should be defined and risk factors identified. Early ICU monitoring should be attempted, especially under the following conditions: (1) lack of clinical response to anti-malarial treatment within 48 h and/or (2) any signs of neurological disturbance (hypoglycaemia excluded). Prospective multicentre trials and guidelines for supportive intensive care are urgently needed.

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L9 ANSWER 29 OF 37 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 97389980 MEDLINE
DOCUMENT NUMBER: 97389980 PubMed ID: 9247032
TITLE: [Nitric oxide and macrophages].
Monoxyde d'azote et macrophages.
AUTHOR: Drapier J C
CORPORATE SOURCE: U 365 INSERM, Section de Recherche, Institut Curie, Paris, France.
SOURCE: PATHOLOGIE BIOLOGIE, (1997 Feb) 45 (2) 110-4. Ref: 73
Journal code: 0265365. ISSN: 0369-8114.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19970922
Last Updated on STN: 19970922
Entered Medline: 19970910

AB **Nitric oxide** (**NO**) is a **gaseous** radical enzymatically produced from L-arginine by virtually every cell. This versatile molecule is involved in a variety of biological functions including defense against pathogens. Micro-organisms whose development is inhibited by **NO** include fungi, bacteria, **protozoa**, helminths and viruses. In murine macrophages, a high output **NO** synthase (NOS II) is regulated transcriptionally by cytokines and microbial products. In the past few years, investigators have identified many other cell types expressing NOS II. However, in human monocytes/macrophages, the existence of the L-arginine-**NO** pathway has long been questioned. Recent findings and new developments in this respect are commented in this short review.

L9 ANSWER 30 OF 37 MEDLINE DUPLICATE 6

ACCESSION NUMBER: 97467676 MEDLINE
DOCUMENT NUMBER: 97467676 PubMed ID: 9326885
TITLE: Leishmania spp.: mechanisms of toxicity of nitrogen oxidation products.
AUTHOR: Mauel J; Ransijn A
CORPORATE SOURCE: Institute of Biochemistry, Chemin des Boveresses 155, Epalinges, Switzerland.
SOURCE: EXPERIMENTAL PARASITOLOGY, (1997 Oct) 87 (2) 98-111.
Journal code: 0370713. ISSN: 0014-4894.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971105
Last Updated on STN: 20000303
Entered Medline: 19971022

AB Intracellular killing of **Leishmania** parasites within activated murine macrophages is thought to result from the toxic activities of nitrogen oxidation products (referred to as **NO**) released by the activated cells. In order to determine possible mechanisms of **NO** toxicity for these microorganisms, promastigotes of **Leishmania** major and **Leishmania** enriettii were exposed to **NO** generated chemically from acidified nitrite, S-nitrosocysteine, diethylamine NONOate, or nitroprusside. Treatment with these agents led to loss of viability (as determined from decreased motility and inhibition of [3H]TdR uptake upon reincubation in **NO**-free medium) with kinetics characteristic for each compound L. major was less sensitive to these effects than L. enriettii, and amastigotes displayed the same sensitivity as promastigotes of the same species. The early effects of **NO** toxicity could be detected within minutes of exposure to the **NO** donors; they included decreased **respiration** rate and inhibition of glucose, proline, and adenine incorporation. Inhibition of the activities of glyceraldehyde 3-phosphate dehydrogenase and of aconitase were also evidenced. In order to determine whether these phenomena reflected the mechanisms of toxicity of bona fide **NO** generated by macrophages, promastigotes were exposed to IFN-gamma + LPS-activated macrophages across permeable membranes. This resulted in marked inhibition of proline and adenine uptake in the parasites, which was restored, however, to control levels when macrophages were activated in the presence of the **nitric oxide** synthase inhibitor NGMMA. These results indicate that several cellular targets may be subject to **NO** toxicity in **Leishmania** parasites, including enzymes of glycolysis and **respiratory** metabolism as well as trans-membrane transport systems.

L9 ANSWER 37 OF 37 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 91131129 MEDLINE
DOCUMENT NUMBER: 91131129 PubMed ID: 2126524
TITLE: Cellular mechanisms of nonspecific immunity to intracellular infection: cytokine-induced synthesis of toxic nitrogen oxides from L-arginine by macrophages and hepatocytes.
AUTHOR: Green S J; Mellouk S; Hoffman S L; Meltzer M S; Nacy C A
CORPORATE SOURCE: Department of Cellular Immunology, Walter Reed Army Institute of Research, Washington, DC.
SOURCE: IMMUNOLOGY LETTERS, (1990 Aug) 25 (1-3) 15-9.
Journal code: 7910006. ISSN: 0165-2478.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199103
ENTRY DATE: Entered STN: 19910405
Last Updated on STN: 19910405
Entered Medline: 19910320

AB **Nitric oxide** (**NO**) produced by cytokine-treated macrophages and hepatocytes plays a vital role in protective host responses to infectious pathogens. **NO** inhibits iron-sulfur-dependent enzymes involved in cellular **respiration**, energy production, and reproduction. Synthesis of L-arginine-derived nitrite (NO2-), the oxidative end product of **NO**, directly correlates with intracellular killing of **Leishmania** major, an obligate intracellular **protozoan** parasite of macrophages: the level of NO2- production is a quantitative index for macrophage activation. The competitive inhibitor of **NO** synthesis, monomethylarginine (NGMMLA), inhibits both parasite killing and NO2- production. For **Leishmania**, the parasite itself participates in the regulation of this toxic effector mechanism. This participation is mediated by parasite induction of tumor necrosis factor alpha (TNF alpha), an autocrine factor of macrophages: **NO** synthesis by interferon-gamma (IFN-gamma)-treated cells can be blocked by monoclonal antibodies to TNF alpha. **NO** production by IFN gamma-treated hepatocytes is of special interest in malaria infections: sporozoite-infected hepatocytes kill the intracellular malaria parasite after treatment with IFN gamma; this killing is inhibited by NGMMLA.

L3 ANSWER 1 OF 1 MEDLINE

ACCESSION NUMBER: 2000244894 MEDLINE
DOCUMENT NUMBER: 20244894 PubMed ID: 10784308
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AUTHOR: Losert H; Schmid K; Wilfing A; Winkler S; Staudinger T; Kletzmayr J; Burgmann H
CORPORATE SOURCE: Department of Internal Medicine I, University Hospital of Vienna, Austria.
SOURCE: INTENSIVE CARE MEDICINE, (2000 Feb) 26 (2) 195-201. Journal code: 7704851. ISSN: 0342-4642.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
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ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000728
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